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Continuous Noninvasive Monitoring of Left Ventricular Function during Exercise by Thoracic Impedance Cardiography Automated Derivation of Systolic Time Intervals

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16. ABSTRACT

Systolic time intervals (ST) obtained during exercise are useful as a method of estimating global left ventricular function. The conventional method, however, which requires a carotid pulse tracing as well as a phonocardiogram of high quality, is technically difficult under conditions of exercise. We have validated a new method of obtaining STI which employs the first derivative of thoracic electrical impedance (DZ/DT). The DZ/DT was recorded using surface electrodes and a microcomputer for automated signal processing. The new method was studied in 20 male normal subjects (aged 18 to 53 years) at rest and during increasing levels of upright exercise. Heart rate ranged from 61 to 173 beats/min. Results obtained simultaneously by both techniques showed no significant difference. Thus impedance cardiography allows continuous monitoring of STI during exercise and may prove to be a valuable addition to multistage stress testing.

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Continuous noninvasive monitoring of left ventricular function during exercise by thoracic impedance cardiography-automated derivation of systolic time intervals

Systolic time intervals (STI) obtained during exercise are useful as a method of estimating global left ventricular function. The conventional method, however, which requires a carotid pulse tracing as well as a phonocardiogram of high quality, is technically difficult under conditions of exercise. We have validated a new method of obtaining STI which employs the first derivative of thoracic electrical impedance (DZ/DT). The DZ/DT was recorded using surface electrodes and a microcomputer for automated signal processing. The new method was studied in 20 male normal subjects (aged 18 to 53 years) at rest and during increasing levels of upright exercise. Heart rate ranged from 61 to 173 beats/min. Results obtained simultaneously by both techniques showed no significant difference. Thus impedance cardiography allows continuous monitoring of STI during exercise and may prove to be a valuable addition to multistage stress testing. (Am Heart J 103:519, 1982.)

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Despite the utility and proven advantages of multistage exercise stress testing,[1-5] there remains a continuing need to improve such techniques. Recent improvements in clinical stress testing including thallium exercise testing[6-8] and radionuclide gated wall motion studies during exercise[9] have improved the sensitivity and specificity of exercise testing to detect significant coronary artery disease (CAD). However, these methods are costly, minimally invasive, and involve some radiation exposure. Previous studies have shown that the first derivative of thoracic electrical impedance (DZ/DT) correlates closely with systolic time intervals (STI) at rest.[10,11] Most previous attempts to analyze STI changes during exercise by the impedance technique have been difficult due to artifacts.[11-14] The present study is an evaluation of a new system designed to monitor DZ/DT during exercise[15] utilizing a microcomputer with algorithms for artifact screening and signal averaging, and automated waveform analysis.

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METHODS

System description. The cardiac exercise stress processor (CESP) automates the determination of exercise STI by monitoring the ECG and DZ/DT waveforms (Fig. 1). The CESP consists of a Minnesota Impedance Cardiograph, a custom analog processor, an Intel System 80 microcomputer, and a Lear Seigler ADM-3A interactive graphic display. The Minnesota Impedance Cardiograph (Model 304A) was modified to expand the ECG frequency response and to provide a conventional three-lead ECG. The microcomputer consists of an Intel SBC 80/20-4 single-board computer, a Burr-Brown MP 8417 data acquisition system, an Intel double-density diskette subsystem, and an Intel SBC-032 random-access memory.

The analog processor interfaces the impedance cardiograph to the microcomputer data acquisition system. It primarily provides calibration adjustment for each analog channel and derives the R wave signal, which is used for detecting the QRS event. The ECG is bandpass-filtered (0.05 to 50.0 Hz) to remove respiratory and electrode baseline shifts and to reduce 60 Hz and high-frequency muscle noise. The filtered ECG is passed through a QRS waveform matching filter (7.2 to 23.4 Hz) to produce the R wave event detection signal. The mean thoracic impedance (Zo) and the impedance cardiogram (DZ/DT) are bandwidth-limited by the Minnesota Impedance Cardiograph and require only amplitude and baseline adjustment by the analog processor.

Real-time exercise acquisition. The exercise program manages the real-time data acquisition, coordinates the exercise protocol, and provides the raw data base archival

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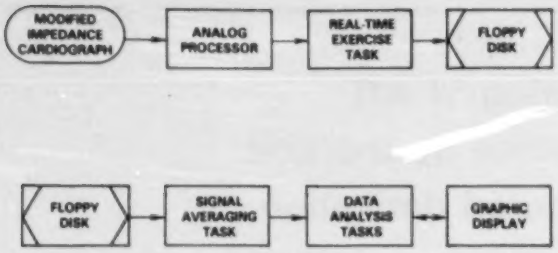

Fig. 1. Block diagram of CESP design illustrating segmentation of real-time and postexercise signal processing functions.

storage. The ECG, DZ/DT, and R wave signals are sampled continuously during exercise at 400 samples/sec using a 12-bit analog-to-digital converter. Additionally, the Zo signal is acquired once per cardiac cycle. According to each signal's calibration range, these data are then adjusted to 10 bits of resolution and stored for subsequent processing. The maximum ADC resolution is 2 μV for the ECG and R wave signals, 2 mohms/sec for the DZ/DT signal, and 40 mohms for the Zo signal.

Each cardiac cycle is triggered by the R wave signal. During system calibration, the CESP attempts to trigger using a default trigger level and alerts the operator for a manual setting if the procedure fails. Thereafter, an adaptive trigger algorithm is employed which sets the trigger level at 50% of the running average R wave peak amplitude. A trigger dead zone prevents false trigger during the T wave and a baseline analysis algorithm raises the trigger level above 50% in the presence of persistent baseline noise. Each of these R wave analyses and trigger adjustments occur in real-time during acquisition of the exercise data. All detected cardiac cycles, regardless of beat-to-beat variation or anomaly, are held in memory for possible storage on floppy disk. Depending upon the selected exercise protocol,[15] the sampled cardiac cycle data within each minute of data acquisition are either discarded or stored on floppy disk. Screening of individual cycles for ensemble averaging is deferred to subsequent data recall and analysis so that all original data are saved for alternative analyses.

Automated STI analysis. The analysis program recalls and averages the acquired cardiac cycle data, performs automated or interactive waveform analysis, manages the data base of averaged cardiac cycles and derived parameters, and facilitates the graphic display of waveforms and parameter response trends. The selection of individual cardiac cycles for ensemble averaging is based on several procedures. During data acquisition the exercise program continuously assembles a table of mean R-R intervals as determined over each successive 30-second period. This mean excludes R-R intervals which vary by greater than one standard deviation (1 SD) on either side of the running mean, as may occur with ectopic ventricular beats. Additionally, should the 30-second period present significant overall R-R interval variance, the period is marked as improper for ensemble averaging and is automatically rejected.

The averaging algorithm is initially set for 64 cycles per ensemble with an increase of 8 cycles/stage for successive stages of the Bruce protocol. This procedure allows for an increase in the available number of cycles per minute (heart rate) and compensates for an expected decrease in signal-to-noise ratio at higher work levels. Prior to each ensemble average, the R-R interval table is referenced to determine the expected R-R interval for the designated exercise averaging period. Then, according to a specified acceptance criteria (12.5% in the present study), a minimum and maximum R-R interval range is calculated and each cardiac cycle is evaluated for inclusion in the ensemble average.

In both the automatic and interactive modes, the averaged ECG and DZ/DT waveforms are then processed to identify certain waveform features for the determination of STI. In the automatic mode, the resultant STI data are accumulated as a graphic trend to permit a rapid assessment of exercise trend response. In the interactive graphics mode, however, the investigator may confirm the accuracy of waveform feature analysis, adjust waveform feature placement, perform other special operations, and ultimately accept or reject the averaged waveform. For this study, the placement of cursors 0, 2, and 4 (Fig. 2) was altered 15% of the time. This was done to ensure that the 0 cursor was placed at the earliest onset of the QRS, that cursor No. 2 was at the onset of the rapid upstroke of DZ/DT, and that cursor No. 4 was placed at the nadir of the DZ/DT waveform.

Exercise protocol. Twenty normal male subjects ranging in age from 18 to 53 years were studied (mean age = 24 years). Each subject was studied at rest, during four stages of gradually increasing exercise, and again in the postexercise recovery period. Heart rate ranged between 61 and 173 beats/min. During each study interval, an ECG, a phonocardiogram (PCG), and carotid pulse (CP) were obtained using a Cambridge multichannel recorder. The CP was recorded with a hand-held transducer (Helige). Only records which were judged to be sufficiently free of artifact were utilized for interpretation. Despite the difficulty of recording STI by these techniques during upright exercise, enough tracings were obtained to allow analysis of each stage in 10 of 20 subjects studied. Results shown are the mean of three separate determinations. STI were then derived in the standard manner described by Lewis et al.[16, 17] (Fig. 3).

Simultaneously with the CP and PCG recordings, the ECG and DZ/DT were acquired throughout exercise using the microcomputer system. A tetrapolar circular electrode system was employed with aluminum band electrodes 0.25 inches wide (3M electrode tape No. M6001). The upper electrode pair was located on the neck and the lower pair was located at the level of the xiphoid process. Both electrode pairs were separated by 3 to 5 cm (Fig. 4). A carrier (4 mamp at 100 kHz) current was passed between

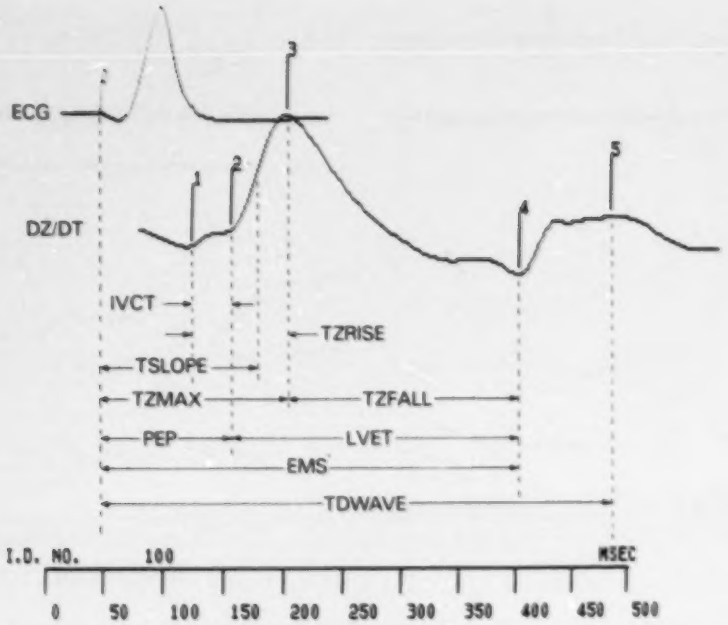

Fig. 2. Cardiac exercise stress processor (CESP) display of averaged electrocardiogram *(ECG)* and impedance cardiogram *(DZ/DT)* with subsequent automated CESP measurements. For abbreviations see legend to Fig. 3.

the two distal electrodes and the inner electrodes detected the voltage. Derivation of STI from the impedance waveform data is illustrated in Fig. 2.

RESULTS

Correlations of automated with hand-measured parameters are shown in Fig. 5. The automated measurements were obtained from the CESP system, and the hand-measured parameters were obtained from simultaneous but separate recordings of CP, PCG, and ECG. In each case, the correlation coefficient was highly significant ($p < 0.001$). Table I shows values (mean ± SD) obtained by both techniques at rest and during various stages of exercise. By the difference-of-means t test, there was no significant difference between any measurement pair ($p < 0.001$). Considering the CESP sampling rate and the Cambridge recorder paper speed, the STI measurement resolutions were ±2.5 msec and ±10 msec, respectively. Therefore any apparent differences in mean values obtained by both techniques fall within measurement error.

DISCUSSION

Origin of impedance waveform and relationship to STI. Impedance cardiography has been utilized for many years and has been shown to be accurate in assessment of resting STI.[10,11] The origin of the impedance waveform has been established to be primarily dependent on aortic systemic flow. A change in aortic volume is the generator of the systolic pulsatile wave. DZ/DT represents a change in aortic velocity, i.e., in ejection velocity; thus the relationship to STI.[11] The impedence cardiogram, traditionally designated as DZ/DT, is actually provided by the Minnesota Impedence Cardiograph. Neither the analog processor nor the digital processor performs differentiation of the signal. Therefore, DZ/DT is perhaps a misnomer since it is simply a bandpass region of the total available thoracic impedence signal. Therefore, any errors traditionally atributed to differentiation do not apply.

Relationship of STI to left ventricular function. In the absence of valvular heart disease and in the presence of normal intraventricular conduction and normal sinus rhythm, STI allow quantification of left ventricular (LV) performance which can be derived totally noninvasively. LV dysfunction characteristically produces lengthening of the preejection period (PEP) and diminution of the LV ejection time (LVET) with little change in electromechanical systole (EMS). The ratio PEP/LVET has been shown

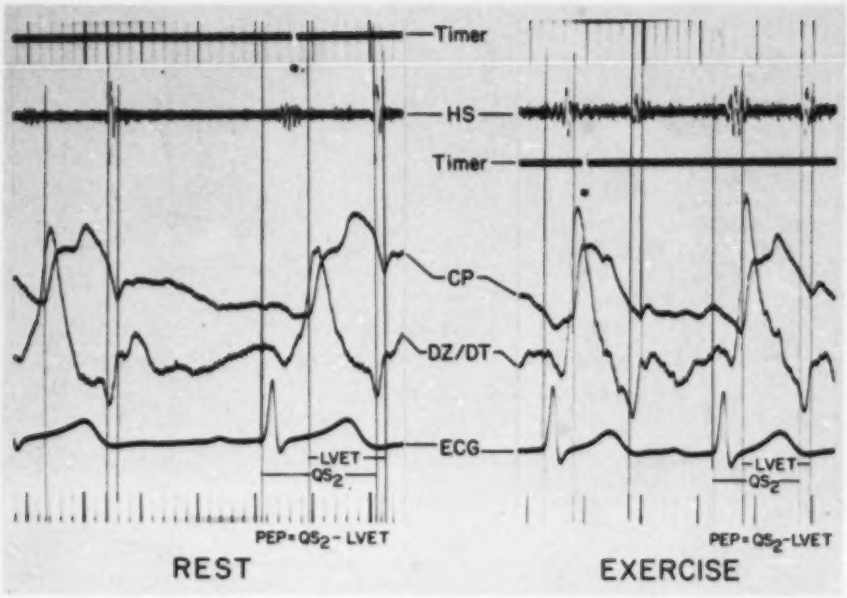

Fig. 3. Simultaneous recording of heart sounds *(HS)*, 1 second calibration pulse *(Timer)*, carotid displacement pulse *(CP)*, impedance cardiogram *(DZ/DT)*, and electrocardiogram *(ECG)* obtained at rest *(left panel)* and during exercise *(right panel)*. Manual measurements are, left ventricular ejection time *(LVET)*, electromechanical systole (EMS = QS_2), and preejection period *(PEP)*.

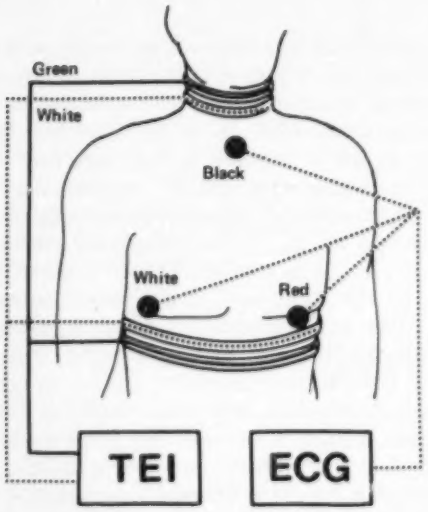

Fig. 4. Schematic representation of thoracic electrical impedance *(TEI)* and electrocardiogram *(ECG)* electrode configuration.

to be valuable as a single expression of global LV performance.[18-20] The ratio has the advantage of reflecting abnormalities when neither component is clearly abnormal. Further, because digitalis shortens both PEP and LVET, the ratio PEP/LVET is more useful than either component alone in patients taking digitalis.[21] Decreased LV performance results in an increase in PEP/LVET which is correlated with cardiac index (CI) and stroke index (SI) in patients with CAD, hypertensive, and primary myocardial disease. Certain studies have suggested that PEP/LVET may be a more sensitive index of LV dysfunction than CI or SI.[22] PEP/LVET has also been found to be closely correlated with LV ejection fraction (EF) determined by angiography ($r = 0.90$, $p < 0.01$).[23] EF, or the extent of ventricular emptying per heart beat, is perhaps the best index of ventricular function and correlates highly with survival in patients with cardiac disease.

Studies of STI during exercise. STI have been measured during exercise previously.[10, 12-14, 24-28] These measurements require considerable care and time in calculating the data once the measurements are made. In addition, several investigators are needed to gather these data, since the acquisition is usually dependent on hand-held transducers and avoidance of motion artifact. Changes in STI that have been described during exercise include an initial decrease in PEP/LVET due to an increase in cardiac output, stroke volume (SV), and contractility, followed by a leveling off of PEP/LVET.[12-14] A slight increase in PEP/LVET may occur due to a decrease in SV (usually only after 70% predicted maximal heart rate).[24]

Some patients with CAD have shown a lengthen-

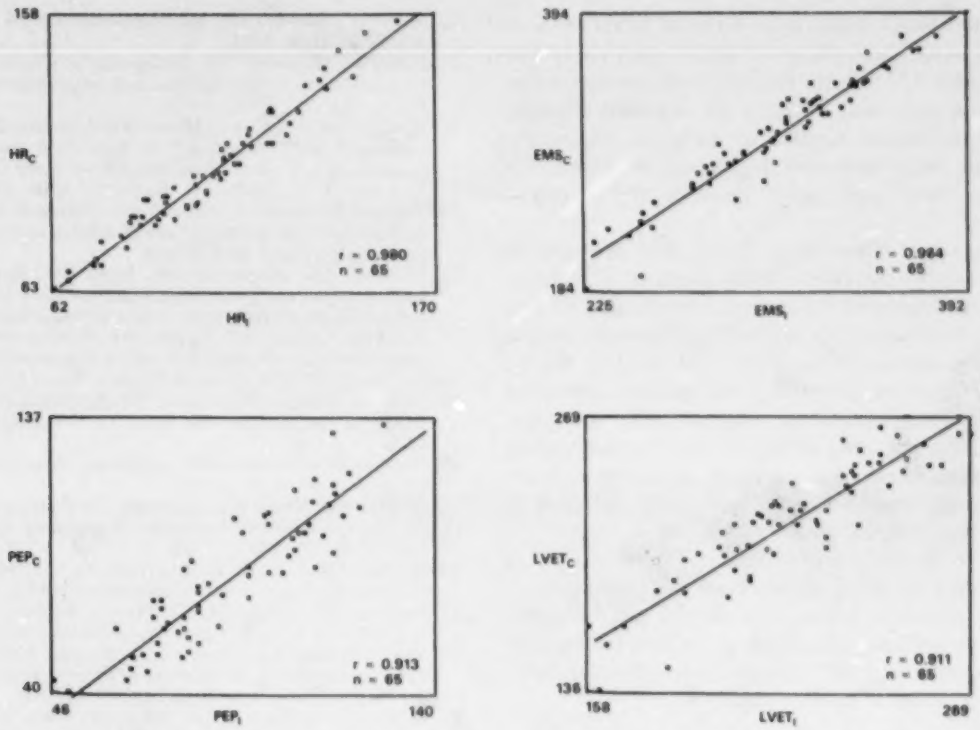

Fig. 5. Correlation of CESP automated or computer generated data *(I)* to traditionally derived data *(C)* using the ECG, carotid pulse, and phonocardiogram. *HR* = heart rate; *EMS* = electromechanical systole; *PEP* = preejection period; *LVET* = left ventricular ejection time. Units are HR = beats/min; EMS, PEP, LVET = msec.

Table I. Comparison of manual and automated STI

	EMS (msec)	*LVET* (msec)	*PEP* (msec)	*PEP/LVET* (msec)
Rest I	358 ± 22	239 ± 21	118 ± 18	0.50 ± 0.08
C	359 ± 25	243 ± 20	116 ± 15	0.48 ± 0.08
Ex_1 I	330 ± 20	241 ± 22	89 ± 12	0.38 ± 0.08
C	329 ± 23	241 ± 26	88 ± 22	0.38 ± 0.12
Ex_2 I	311 ± 22	230 ± 23	81 ± 12	0.35 ± 0.08
C	312 ± 28	236 ± 24	75 ± 18	0.32 ± 0.08
Ex_3 I	291 ± 28	216 ± 25	75 ± 12	0.36 ± 0.09
C	284 ± 31	212 ± 24	72 ± 17	0.34 ± 0.09

Abbreviations: I = ECG and DZ/DT automated measurement values; C = ECG, CP, and PCG hand-measured values; Ex_1, Ex_2, Ex_3 = exercise levels 1, 2, and 3.

ing of LVET, presumably due to impaired LV performance or increased afterload,[27, 31] or to an increase in PEP/LVET at earlier stages of exercise, typical for LV failure.[24, 28, 29] In one study,[24] all patients with angina during exercise showed an increased PEP/LVET at an earlier stage of exercise than normals. These abnormalities identified patients with CAD in whom no significant ischemic ECG changes occurred. Pouget et al.[27] studied 20 patients with angina and 20 matched normal controls. Marked prolongation of LVET after exercise reflecting ventricular dysfunction was found in their patients with angina and was not found in their normals or in patients with nonanginal chest pain, implying a sensitivity and specificity of 100% for this technique to detect CAD. Balasubramanian et al.[32] measured mean thoracic impedance (in ohms) during upright treadmill exercise and found a decrease in impedance during exercise correlating with the extent of ST segment depression. This was

attributed to an increase in thoracic blood volume and pulmonary extravascular water, most likely due to transient LV failure. Patients with preexcitation syndrome and false positive ST segment changes showed responses similar to normals, suggesting that this technique may be useful to distinguish between true and false positive ST segment changes.[32]

Conclusions. Thus it is likely that changes in impedance do correlate with changes in cardiac function. The chief value and contribution of the present technique is its capability to provide continuous monitoring of the ECG and DZ/DT during exercise, thereby permitting automated derivation of STI. Trend plots for exercise STI are then displayed graphically as part of the exercise testing procedure. There are no hand measurements or calculations involved, and hard copy printout is available at the end of the exercise test.

This study has demonstrated the validity of these measurements in upright exercise in a population of normal controls. These data should not be interpreted to indicate that changes in these parameters will necessarily reflect changes in ventricular function in a group of cardiac patients.

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JOURNAL ARTICLE

CONTINUOUS NONINVASIVE MONITORING OF LEFT VENTRICULAR FUNCTION DURING EXERCISE BY THORACIC IMPEDANCE CARDIOGRAPHY-AUTOMATED DERIVATION OF SYSTOLIC TIME INTERVALS

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